



PATENT
Attorney Docket No.: JAL1100-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A. Battaglia Art Unit: 1617
Application No.: 10/053,313 Examiner: T. J. Criares
Filed: January 18, 2002
Title: GUM RESIN AS A CARRIER FOR TOPICAL APPLICATION OF
PHARMACOLOGICALLY ACTIVE AGENTS

Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Alex Battaglia, M.D., Ph.D., do hereby declare and state that:

1. I presently hold the position of CEO of Jaleva, Inc., having a place of business at 8033 Paseo del Ocaso, La Jolla, CA 92037.

2. I hold a Doctor of Medicine (M.D.) degree granted by Columbia College of Physicians and Surgeons, New York, in 1993, as shown in my resume, attached herewith. I also hold a degree of Ph.D. in Molecular Pathology granted by University of California, San Diego, in 2002.

3. Jaleva, Inc. is the Assignee of 100 percent interest in U.S. Application Serial No. 10/053,313, filed January 18, 2002, entitled GUM RESIN AS A CARRIER FOR TOPICAL APPLICATION OF PHARMACOLOGICALLY ACTIVE AGENTS.

4. I am familiar with the contents of the above-identified application, and have reviewed the Office Action dated February 3, 2004. I understand that the Examiner has rejected

Applicant: A. Battaglia
Application No.: 10/053,313
Filed: January 18, 2002
Page 2

specification fails to recite other solvents that would have the effect of causing the pharmacologically active agent to remain on the skin other than the solvent ethanol. I further understand that the Examiner has rejected claims 1-13 and 29-32 under 35 U.S.C § 103(a) for allegedly being unpatentable over Goh et al., (Reference D1), stating that it would have been obvious to the skilled artisan to form the composition of PB and ethanol since the antiviral compound podophyllin in tincture benzoin is a conventional composition and ethanol was less irritating. The Examiner also alleges that it would have been obvious to leave the composition disclosed in the cited reference on the skin for a prolonged period of time (i.e., greater than six hours).

5. With respect to the §112 rejection, please consider the following. A volatile solvent is used to dilute the gum resin of choice to effect a final desired concentration/viscosity of the composition. Following application of the composition to the skin, the volatile solvent evaporates to leave a hydrophobic coating comprised of the gum resin and the pharmacological agent. As disclosed on page 6, lines 18-19 of the specification as filed, "volatile solvents for use in the subject compositions include alcohols such as methanol, ethanol, propanol, and isopropanol, and ketones, such as acetone. Other topically acceptable volatile solvents may be used in the compositions as well."

6. It is therefore reasonable to expect that the solvents listed above are interchangeable and that other alcohols, for example methanol or propanol, and ketones, for example acetone, would serve the same purpose. Ethanol was merely an example of the plurality of volatile solvents useful in the compositions of the invention.

Applicant: A. Battaglia
Application No.: 10/053,313
Filed: January 18, 2002
Page 3

7. With respect to the § 103(a) rejection, please consider the following. The cited reference describes the efficacies of 0.5% podophyllin resin in ethanol (PE 0.5%); 0.25% podophyllin in ethanol (PE 0.25%); and 25% podophyllin in tincture benzoin (PB) for the treatment of penile warts. A comparison of the treatments was used to ascertain whether PE causes less skin irritation than PB. The study recognizes that podophyllin resin is toxic and must be removed from the skin by rigorous washing 1-6 hours post-application. The scope of the reference is to identify a composition that minimizes the toxic effects of the podophyllin. Therefore it is not obvious to a skilled artisan to simply leave a composition of the cited reference on the skin of a patient for a period longer than six hours. Doing so will cause severe skin irritation, including lesions, which is hardly an acceptable treatment for penile warts.

8. The compositions of the subject invention avoid the problems addressed by the cited reference by teaching the use of pharmacological agents that are efficacious without being locally or systemically toxic or caustic to the skin of the patient. Applicant's claimed compositions are intended to remain at the site of application for at least 6 hours and more often 8 to 72 hours depending on the treatment.

9. As stated above, the study compares the efficacies of three compositions containing different concentrations of podophyllin for the treatment of penile warts, and concludes that PE is equally as efficacious as PB, with a lower incidence of side effects. The reference suggests that a lower concentration of PB may equally reduce contact dermatitis.

10. The addition of ethanol would still yield a mixture that contains benzoin. Thus, once the ethanol evaporates, the toxic agent, i.e. PB, is in constant contact with the skin. There is no motivation to add ethanol to PB at all when Goh et al. clearly observed that PE, in the

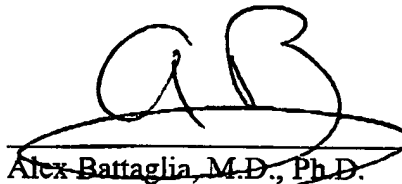
PATENT
ATTORNEY DOCKET NO.: JAL1100-1

Applicant: A. Battaglia
Application No.: 10/053,313
Filed: January 18, 2002
Page 4

absence of benzoin, is a superior treatment for penile warts. Therefore it is not obvious to the skilled artisan to try to add ethanol to PB given the results presented by the cited reference.

11. I further declare that all statements made herein of knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: March 18, 2004



Alex Battaglia, M.D., Ph.D.

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PERSONAL INFORMATION

NAME: ALEX S. BATTAGLIA, M.D., Ph.D.

BUSINESS ADDRESS: Southern California Permanente Medical Group
Dept. Head and Neck Surgery, Otology and Neurotology
3033 Bunker Hill Street
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W: (858) 581-8204 Fax: (858) 581-8228
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HOME ADDRESS: 8033 Paseo Del O'Caseo
La Jolla, CA 92037
W: (858) 456-6221 Fax: (858) 792-1411

BIRTH: August 28, 1964; Berkeley, CA

FAMILY: Wife: Eva Beim Battaglia; Profession: V.P. Marketing Jaleva, Inc.
Son: Jordan Marc Battaglia; Born 8/14/98

EDUCATION

HIGH SCHOOL: Berkeley High School; Berkeley, CA 1978-1982

UNDERGRADUATE: University of California; Berkeley, CA 1984-1986
B.A. Environmental Science
Reed College 1982-1984

MEDICAL SCHOOL: Columbia College of Physicians and Surgeons 1990-1993
Dartmouth Medical School; Class Rank: Upper 1/3 1988-1990

INTERNSHIP: University of California, San Diego; San Diego, CA 1993-1994
Department of Surgery

RESIDENCY: University of California, San Diego; San Diego, CA 1994-2000
Division of Otolaryngology-Head and Neck Surgery
In Service Scores: 97th% (1997), 91st% (1998)

FELLOWSHIP: Neurotology, The Otology Group; Nashville, TN 2000-2001
Preceptor: C. Gary Jackson, M.D.

GRADUATE SCHOOL: University of California, San Diego; San Diego, CA 1996-2002
Dept. Molecular Pathology, PI: Allen F. Ryan, Ph.D.
Ph. D. Dissertation: *Ras Contributes to Outer Hair Cell Apoptosis in the Basal Turn of the Cochlea after Cisplatin and Gentamicin Exposure*

HONORS & AWARDS:	Voted 3 rd Best Doctor in La Jolla, CA (La Jolla Light 10/31/02)	2002
	Kaiser Dept. Head and Neck Surgery Merit Award	2002
	UC San Diego Dept. General Surgery Teaching Award	2000
	The Deafness Research Foundation Resident Research Grant: \$45,000 <i>The Role of Integrins in the Development of the Inner Ear II</i>	1998-2000
	The Triologic Society Resident Research Training Award: \$25,000 <i>The Role of Integrins in the Development of the Inner Ear I</i>	1997-1998
	Association for Research in Otolaryngology Resident Travel Award	1997
	National Institutes of Health: NIDCD IRTA Fellowship Supervisor: Dr. David J. Lim	1992-1993
	Excellence Award for Academic Assistance, Dartmouth	1990
	UC Berkeley Academic Honors	1985
	R.F. Arragon Award for Academic Excellence, Reed	1982
	Italian/American Federation Scholarship	1982
	California Scholarship Federation life member	1982
	Excellence in Youth Award-Mayor of Berkeley	1981
	Distinguished Service Award for saving a life (Berkeley)	1980

LICENSURE: California, Tennessee, and Nevada.

PRIOR HOSPITAL APPOINTMENTS:

Attending Staff, Division of Otology/Neurotology,
Metropolitan Nashville General and Vanderbilt Hospitals,
Nashville, TN, 2000-2001.

RESEARCH EXPERIENCE OUTSIDE OF DISSERTATION

Principal Investigator, Southern California Kaiser Permanente, Intratympanic Dexamethasone for Sudden Sensorineural Hearing loss: An IRB Approved, Blinded, Multi-Center, Placebo-Controlled, Prospective, Randomized Trial, 10/03- present.

Fellow, National Institutes of Health, National Institute of Deafness and Communication Disorders, Laboratory of Cellular Biology; Supervisor: Dr. David J. Lim. Studied vesicular traffic around the cuticular plate of hair cells, 5/92-5/93.

Research Assistant, California Institute of Technology; Principal Investigator: Dr. Jean-Paul Revel. Immunolocalized rat heart gap junction proteins, 1/87-5/88.

SOCIETY MEMBERSHIPS

NATIONAL: American Neurotologic Society
American Academy of Otolaryngology-HNS
Academy of Facial Plastic and
Reconstructive Surgery
Association for Research in Otolaryngology

MEETINGS ATTENDED: American Academy of OTO-HNS; 1994, 1995, 1998, 2002
Association for Research in Otolaryngology; 1993, 1997, 1998
COSM; 2003
Otology and Neurotology Update; 1998, 2002

PRESENTATIONS: *A G-Protein Mediates Hair Cell Susceptibility to Gentamicin.*
Presented at AAO-HNS, San Antonio, TX, 1998; ARO,
St. Petersburg, FL, 1998.

A Dominant Negative Integrin Mutant Disrupts Spiral Ganglion Neurite Extension. Presented at ARO,
St. Petersburg, FL, 1997.

UC San Diego Division of Otolaryngology Grand Rounds:

- 2002 Ras Contributes to Outer Hair Cell Apoptosis in the Basal Turn of the Cochlea after Cisplatin and Gentamicin Exposure
- 2000 Treatment of Chronic Otitis Externa: Science or Voodoo?
- 1999 Laryngeal Fractures
- 1998 Paradoxical Vocal Cord Movement
- 1998 Diagnosis and Treatment of Fungal Sinusitis
- 1997 A G-Protein Mediates Hair Cell Susceptibility to

Gentamicin.
1997 The History of Local Flaps: Claude Dufourmental
1996 Head and Neck Manifestations of Tuberculosis
1996 The Pathogenesis of Otosclerosis
1995 A Dominant Negative Integrin Mutant Disrupts
Spiral Ganglion Neurite Extension
1995 The Etiology of Meniere's Disease
1994 Surgical Management of Head and Neck Melanoma
1994 Epistaxis: Surgical Management vs. Embolization

TEACHING EXPERIENCE

Course Faculty, Temporal Bone Surgical Dissection:
UCSD Temporal Bone Course, San Diego, CA: 5/2002
The Ear Foundation, Nashville, TN: 8/2000, 10/2000, 11/2000.

Facial Plastics and Techniques in Local Reconstruction,
San Diego, CA, 1996, 1997.

Laboratory dissections and didactic lectures – Head and Neck Anatomy
Course, University of California, San Diego Medical School, 1994.

COURSES ATTENDED

Local Flaps and Reconstruction, San Diego, CA, 2000.
Course Director: Debbie Watson, M.D.

Maxillofacial Plating Yearly Courses, San Diego, CA, 1997-2000.

Temporal Bone Anatomy Course, San Diego, CA, 1996, 1998, 2000.
Course Director: Jeffrey Harris, M.D., Ph. D.

Aesthetic Laser Surgery, San Diego, CA, 1995.
Course Director: Terrence Davidson, M.D.

Superficial Anatomy and Cutaneous Surgery,
San Diego, CA, 1994. Course Director: Hugh Greenway, M.D.

PATENTS PENDING

#'s 20030068331 and #20030099666 on www.uspto.gov.

START-UP BUSINESS

CEO Jaleva, Inc. devoted to selling Stayzon™.

PERSONAL

Guitarist/Songwriter/Producer on Folk Rock CD 'Evaluation'.
Biked solo across U.S. Private Pilot. Scuba Diver.
Backpack. Rugby. Speak French. Published poet.

PUBLICATIONS

PAPERS:

- Battaglia A.**, Bodmer D., Brors D., Pak K., Frangos J.A., Ryan A.F.: Involvement of RAS activation in toxic hair cell damage of the mammalian cochlea. *Neuroscience*, 122(4):1025-35, 2003.
- Battaglia A.**, McGrew B., Jackson C.G.: Reconstruction of the Entire Ossicular Chain. *Laryngoscope*, 113(4):654-8, 2003.
- Battaglia A.**, Sabri A., Jackson C.G.: Surgical Management of Cholesteatoma in the Only Hearing Ear. *Laryngoscope*, 112:681-85, 2002.
- Battaglia A.**, Merati A., Magit A.: Cherubism: A Difficult Airway. *Otolaryngol. Head Neck Surg.*, 122(4):573-574, 2000.
- Battaglia A.**, Magit A.: Nager Acrofacial Dysostosis with Autosomal Dominant Inheritance: Implications for the Otolaryngologist and Geneticist. *Otolaryngol. Head Neck Surg.*, 123(2):276-277, 2000.
- Battaglia A.**, Ross B., Ryan A.F.: A Dominant Negative Integrin Mutant and Kistritz Disrupt Spiral Ganglion Neurite Extension. *Molecular and Cellular Neuroscience*, In Preparation.
- Ryan A.F., Pak K., Low W., **Battaglia A.**, Mullen L., Harris J.P., Keithley E.M.: Immunological damage to the inner ear: current and future therapeutic strategies. *Adv ORL*. 59:66-74, 2002.
- Dazert S., **Battaglia A.**, Ryan A.F.: Transfection of Neonatal Rat Cochlear Cells In Vitro with an Adenovirus Vector. *International Journal of Developmental Neuroscience*. 15(4-5):595-600, 1997.
- Kachar B., **Battaglia A.**, Jaeger R., Fex J.: Compartmentalized Vesicular Traffic around the Hair Cell Cuticular Plate. *Hearing Research*. 107(1-2):102-112, 1997.

CHAPTERS:

- Battaglia A.**, Lim D, Friedman R, Ryan A.F.: Molecular Biology and Clinical Otology. In: *Clinical Otology*, eds. G. Hughes, M. Pensak, Thieme, New York, pp.53-71, 1997.
- Sabri A., **Battaglia A.**, Jackson C. G.: Surgical Management of Otologic Disease. In: *Medical Handbook for Audiologists*, ed. Smith E., Singular Publishing, New York, pp.1-34, 2001.

DISSERTATION:

Battaglia, A.: Ras Contributes to Outer Hair Cell Apoptosis in the Basal Turn of the Cochlea after Cisplatin and Gentamicin Exposure. University of California, San Diego, Department of Molecular Pathology, pp. 1-149, 2002.

ABSTRACTS:

Battaglia A., Kayali A., Frangos J., Ryan A.F.: Ras Activation Contributes to Outer Hair Cell Susceptibility to Cisplatin and Gentamicin. ARO Abstracts, 2001.

Battaglia A., Parhizkar N., Webster N., Frangos J., Ryan A.F.: A G-Protein Mediates Hair Cell Susceptibility to Gentamicin. ARO Abstracts, 1998.

Battaglia A., Ross B., Ryan A.F.: A Dominant Negative Integrin Mutant Disrupts Spiral Ganglion Neurite Extension. ARO Abstracts, 1997.

Pak K., Sahakian A., **Battaglia A.**, Philip A., Brors D., Ryan A.F.: Gentamicin treatment increases expression of mRNA encoding the proapoptotic factor BAD in the organ of Corti, ARO Abstracts, 2002.

Ryan A.F., Pak K., **Battaglia A.**, Yang G., Harris J.P., Keithley E.: Immunologic damage to the inner ear: current and future therapeutic strategies. 2nd International Symposium on Pharmacotherapy of the Inner Ear. Munich, Germany, Oct 2000.

Ryan A.F., **Battaglia A.**, Dazert S., Jung H.H., Luo L., Dulon D.: Molecular basis of protection and repair of the organ of Corti. Nordisk Oto-Laryngology XXVI Congress, Tampere, Finland, Aug 1996.

POSTER ABSTRACTS:

Battaglia A., McGrew B., Jackson C.G.: Reconstruction of the Entire Ossicular Chain. COSM, Nashville, TN, 2003.

Battaglia A., Merati A., Magit A.: Cherubism: A Difficult Airway. AAO-HNS, Washington D.C., 1995.

Battaglia A., Gill S., Grundfast K.: The Audiology and Cochlear Histopathology of Transgenic Mice with a Melanocyte Anomaly. AAO-HNS, San Diego, CA, 1994.

Battaglia A., Ahn J., Burgoyne J., Keen M.: The Frontal Screw: A New Technique for Suspending and Immobilizing Commminuted Mid-Face Fractures in Edentulous Patients. AAFPRS, San Francisco, CA, 1993.

Kachar B., **Battaglia A.**, Fex J.: Vesicular Traffic around the Cuticular Plate of Hair Cells. ARO, St. Petersburg, FL, 1993.

Pak K., Sahakian A., **Battaglia A.**, Philip A., Brors D., Ryan A., Gentamicin treatment increases expression of mRNA encoding the proapoptotic factor BAD in the organ of Corti. ARO, St. Petersburg, FL, 2003.

ACKNOWLEDGED TECHNICAL ASSISTANCE:

Yancy S.B., John S.A., Ratneshwar L., Austin B.J., Revel J.P.: The 43-kD Polypeptide of Heart Gap Junctions: Immunolocalization (1), Topology (2) and Functional Domains (3). Journal of Cell Biology. 108(6):2241-2254, 1989.

OTHER PUBLICATIONS

Battaglia A.: Louisiana Vulcan. In: Reflexions, 1:2, 1991.

Battaglia A.: The Alameda County Flood Control District Seasonal Wetlands in Union City: A Question of Action. In: S.F. Bay Natural Processes and Cultural Impacts, University of California, Berkeley, Department of Environmental Science, pp.131-136, 1986.

REFERENCES

Available upon request.